Split Liver Transplantation

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Objective

This study reviews the indications, technical aspects, and experience with ex vivo and in situ split liver transplantation.

Background

The shortage of cadaveric donor livers is the most significant factor inhibiting further application of liver transplantation for patients with end-stage liver disease. Pediatric recipients, although they represent only 15% to 20% of the liver transplant registrants, suffer the greatest from the scarcity of sizematched cadaveric organs. Split liver transplantation provides an ideal means to expand the donor pool for both children and adults.

Methods

This review describes the evolution of split liver transplantation from reduced liver transplantation and living-related liver transplantation. The two types of split liver transplantation, ex vivo and in situ, are compared and contrasted, including the technique, selection of patients for each procedure, and the most current results.

Results

Ex vivo splitting of the liver is performed on the bench after removal from the cadaver. It is usually divided into two grafts: segments 2 and 3 for children, and segments 4 to 8 for adults. Since 1990, 349 ex vivo grafts have been reported.

Until recently, graft and patient survival rates have been lower and postoperative complication rates higher in ex vivo split grafts than in whole organ cadaveric transplantation. Further, the use of ex vivo split grafts has been relegated to the elective adult patient because of the high incidence of graft dysfunction (right graft) when placed in an emergent patient. Reasons for the poor function of ex vivo splits except in elective patients have focused on graft damage due to prolonged cold ischemia times and rewarming during the long benching procedure. In situ liver splitting is accomplished in a manner identical to the living donor procurement. This technique for liver splitting results in the same graft types as in the ex vivo technique. However, graft and patient survival rates reported for in situ split livers have exceeded 85% and 90%, respectively, with a lower incidence of postoperative complications, including biliary and reoperation for bleeding. These improved results have also been observed in the urgent patient.

Conclusion

Splitting of the cadaveric liver expands the donor pool of organs and may eliminate the need for living-related donation for children. Recent experience with the *ex vivo* technique, if applied to elective patients, results in patient and graft survival rates comparable to whole-organ transplantation, although postoperative complication rates are higher. *In situ* splitting provides two grafts of optimal quality that can be applied to the entire spectrum of transplant recipients: it is the method of choice for expanding the cadaver liver donor pool.

Because donor liver shortage has been the rate-limiting step in the expansion of hepatic transplantation, several innovative techniques have been developed to enlarge a relatively constant pool of organs. These recently advanced procedures have focused on using a part of the liver allograft for transplantation. Nowhere has this effort been felt more strongly than in pediatric liver transplantation. Al-

though liver replacement in children accounts for only 10% to 15% of all liver transplants performed, the number of whole-organ cadaveric grafts size-matched for this population is inadequate. Because of this quantitative disparity between donors and recipients, the pretransplant mortality rate has historically been reported to be as high as 25% to 50% in children.¹

To maximize donor organ use in children and small adults, three procedures have evolved from the fundamental principle that a component of the liver with a suitable vascular pedicle, bile duct, and venous drainage, along with sufficient functional hepatocyte mass, can sustain hepatic function in a patient as well as a whole organ. Reduced liver transplantation (RLT) was the wellspring for this effort, first

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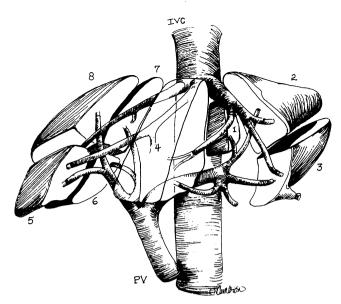


Figure 1. Segmental anatomy of liver. Segment 1: caudate liver. Segments 2 through 4: left lobe. Segments 5 through 8: right lobe. Split liver grafts usually comprise segments 2 and 3 and segments 4 through 8.

reported by Bismuth and Houssin in 1984.² Because of its segmental anatomy, the liver can be separated into several independent anatomic units, each of which can be transplanted (Fig. 1). In RLT, the liver graft can be tailored on the bench to a variety of functional lobes or segments. The most commonly employed parts of a graft used in children are segments 2 and 3 (left lateral segment) and segments 2, 3, and 4 (left lobe). Because of size discrepancy, the extended right lobe, segments 4 to 8, is rarely used in pediatric patients. In RLT, when either a segment 2 and 3 graft or a segment 2 to 4 graft is used, the remaining right lobe is discarded. Results with RLT in children have been comparable to those reported when whole-organ cadaveric grafts are used.3-5 Further, advocates of the procedure cite the lower incidence of hepatic arterial complications due to the larger caliber of the adult hepatic artery.^{6,7} However, although RLT increases the number of pediatric donor organs, this technique does not increase the total number of organs available for transplantation; indeed, it actually disadvantages the adult recipient pool, which has grown 12.1-fold during the past 8 years.8

Living-related donor (LRD) liver transplantation (LRD) is a natural extension of RLT. Use of a portion of the liver from a living donor was attempted by Raia et al in 1988 and first successfully carried out by Strong et al in 1989. During the past 10 years, approximately 1000 LRD transplants have been performed throughout the world, achieving graft and patient survival rates equivalent or better than those observed with cadaveric whole organs or RLT. The advantages of LRD include selection of an ideal donor in whom liver graft function is immediate, and the ability to schedule the case electively, allowing maximal preparation of the recipient. However, the potential advantages of increased histocompatibility between donor and recipient, fa-

voring a lower incidence of rejection, have not been realized. LRD transplantation has also been recently applied to adults in selected cases. ^{11,12} Despite the success observed in pediatric LRD, there are still unresolved issues concerning the risks posed to donors, who are usually parents. To date there have been at least two known donor deaths after LRD. ¹³

Split liver transplantation (SLT) is the culmination of the stepwise progression from RLT and LRD. With this technique, a whole adult cadaveric liver is divided into two functioning allografts. This procedure not only overcomes the drawbacks of RLT and LRD but also increases the total number of donor organs. In fact, full development of SLT may render RLT and LRD obsolete, except in unusual or emergent circumstances. Further, SLT may be able to provide enough liver grafts for the entire pediatric recipient pool. This review will focus on the current status of SLT and the role of this procedure in expanding the liver donor pool.

SPLIT LIVER TRANSPLANTATION

Pichlmavr et al14 in 1988 reported the first clinical attempt at SLT, placing a right graft into a 63-year-old woman with primary biliary cirrhosis and the left graft into a small child with biliary atresia. One year later, Bismuth et al¹⁵ described two patients with fulminant hepatic failure, each receiving a split graft. Although both patients recovered from coma with improvement of liver function, death occurred from multiple organ failure on postoperative day 20 in one, and from diffuse cytomegalovirus disease on postoperative day 45 in the other. The authors claimed that neither poor graft function nor technical problems contributed to the patients' death. Broelsch et al¹⁶ reported the first series of 30 SLT procedures in 21 children and 5 adults. In this early experience, patient survival was inferior to reported series¹⁷ of whole-organ cadaveric liver transplants: only 67% of the children and 20% of the adults who received split grafts survived. Technical problems were common, with a retransplant rate of 35% and a biliary complication rate of 27%.

Despite some skepticism about the lasting role of SLT in decreasing the donor shortage, and because of the less-than-satisfactory results obtained in early cases, several European centers, faced with increasing numbers of deaths of waiting-list patients because of donor scarcity, cautiously pursued the SLT option.

A collective experience of 50 donor livers, providing 100 grafts during a 5-year period, was reported from the European Split Liver Registry by de Ville. ¹⁸ In this series, graft and patient 6-month survival rates were stratified according to elective or urgent status of the patient. In the former situation, survival rates for graft and patient were 80% and 88.9% for children and 72.2% and 80% for adults, respectively. In the urgent setting, graft and patient survival rates were 61.3% and 61.3% for children and 55.6% and 67.7% for adults. Twenty split grafts were lost because of compli-

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Table 1. REVIEW OF EX VIVO SPLIT LIVER SERIES

Author				Patient Survival (%)	Graft Survival (%)	BC (%)
	Year	Graft #	%HR			
Emond	1990	18	28	67	50	27
Broelsch	1990	30	40	60	43	27
Shaw	1990	10	70	50	50	40
Otte	1990	4		50	50	0
Houssin	1993	16	56	75	69	25
Sloof	1995	15		73	67	
Otte	1995	29	27	71	67	17
de Ville	1995	98	33	68	62	23
Bismuth	1995	30	7	93	90	23
Bismuth	1996	27	4	79	78	22
Broelsch	1996	19	58	63	58	16
Kalayoglu	1996	12	8	91	75	25
Rela	1998	41	12	90	88	14.6

HR, high-risk patient; BC, biliary tract complication.

cations related to the graft itself; technical complications included hepatic artery thrombosis (11.5%), portal vein thrombosis (4%), and biliary complications (18.7%). These results were compared with the European Liver Transplant Registry of conventional orthotopic liver transplantation performed during the same time period and did not show a significant difference. In fact, although adult patients receiving a split graft electively had twice the retransplant rate as those with a whole graft, patient survival was higher in the former group (88.9% vs. 80.3%). Children who received a split graft electively actually had lower graft loss and retransplantation rates.

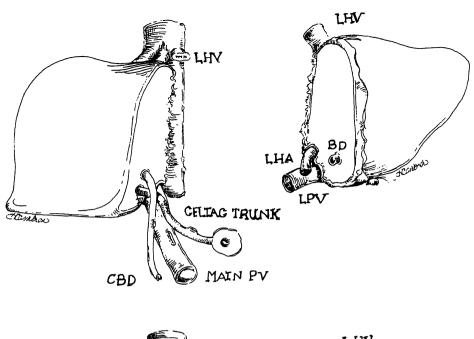
The results described from the European Split Liver Registry stimulated renewed interest in SLT, as evidenced by more recent series reported by Azoulay, 19 Otte, 20 Kalayoglu,²¹ and Rela²² and their colleagues. In all of these later series, selection of high-risk patients appeared to be the dominant factor influencing poor outcome. Further, this effect was more pronounced in recipients of right grafts. As shown in Table 1, the median percentage of high-risk patients receiving transplants in the series that reported clinical condition was only 28%, and several transplant centers have made specific efforts to avoid transplanting high-risk patients with split liver grafts. This has been emphasized for adult patients by the King's College Group, 18 who state, "Our policy is not to split a liver for an ICU-based adult patient, but to give a full-size graft." Based on the 349 cases reported and shown in Table 1, it appears that although patient selection undoubtedly plays an important role in graft and patient outcome, other factors directly or indirectly related to the splitting must also be considered to account for some of the unique complications associated with split grafts when they are used in more urgent patients, particularly adult recipients. Further, if SLT is to be offered to the entire spectrum of patients in need of liver replacement, further improvement in the technique is required.

The remainder of this review will address the two basic types of SLT that been performed clinically, ex vivo and in situ, and will compare and contrast the results.

EX VIVO TECHNIQUE

In the ex vivo split liver technique, the whole organ is retrieved and preserved with University of Wisconsin (UW) solution according to standard techniques of multiple organ procurement. Grafts are prepared at the recipient transplant center in an ice bath of UW solution. Predissection cholangiography and arteriography, to delineate the anatomy more precisely, are performed in some centers^{19,23}; others have not found this step necessary. 21,22 In the latter, a metal cannula is used to probe the hepatic artery and bile duct gently to facilitate detection of aberrant anatomy. Dissection of the portal triad is performed to separate the branches of the hepatic artery, portal vein, and right and left hepatic ducts. Opinions vary as to which liver half should retain the entire hepatic/celiac trunk and main portal vein. In all cases, the common bile duct is retained with the right graft (Figs. 2 and 3).

The rationale for determining which graft should receive the major vascular pedicle is explained by the anatomy of the components of the porta hepatis. ²⁴ In most cases, the left portal vein and right hepatic artery should be sectioned because they are longer, thus facilitating the anastomoses to the recipient vessels. Absence of a portal vein bifurcation is a contraindication to liver splitting. Because microsurgical hepatic artery reconstruction is now commonly performed, sectioning the left hepatic artery to remain with the left graft is preferred, as is done in *in situ* splitting. The left hepatic duct is preferably sectioned because it is absent in only 2% to 9% of patients. When the left hepatic duct is absent, it immediately branches to drain segment 4 and segments 2 and 3, allowing a favorable plane of transection between



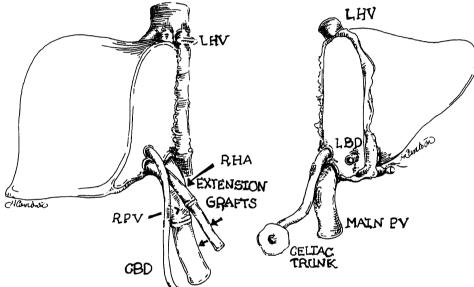


Figure 2. Schematic representation of preparation of each split graft. Top view shows the celiac trunk, main portal vein, and common bile duct with a right graft. The left graft has the sectioned left hepatic artery, left portal vein, and left bile duct. Bottom view shows a right graft with the sectioned right hepatic artery, right portal vein, and common bile duct. Extension grafts are sewn to the right portal vein and right hepatic artery on the back table. The left graft has main vessel trunks and left hepatic duct.

segment 4 and segments 2 and 3. A single right hepatic duct is less common and divides into two ducts in 30% to 50% of cases, thus making division of the right duct more problematic.

Interposition grafts consisting of allogeneic iliac artery, splenic or superior mesenteric artery, and the iliac vein have been used as extensions to both right and left sides. The line of parenchymal transection extends from the confluence of the middle and left hepatic veins to approximately 0.5 to 1 cm to the right of the umbilical fissure up to the hilar plate. Dissection is usually done with mosquito fracture technique or scalpel transection with ligation of the intrahepatic portal triad structures. The hepatic veins are dissected, retaining the left hepatic vein with the left graft and the right and middle hepatic veins in continuity with the vena cava with the right graft. The cut surfaces of the grafts are often sealed

with fibrin glue, reinforced with collagen or polyglactin 910 mesh, to reduce bleeding. 19

Implantation of the right split into an adult is accomplished in the standard orthotopic manner with or without venovenous bypass. Despite oversewing of the left hepatic vein orifice, the suprahepatic vena caval cuff is not compromised in width and fits easily to the recipient cuff. As discussed above, if the right hepatic artery and right portal vein are sectioned with the right lobe, interposition vascular grafts must be used for anastomosis to a suitable source of inflow. Biliary reconstruction is usually choledocholedocostomy with a T tube. Decompression with a T tube prevents bile leakage from the cut surface of the liver.²⁵

The left graft is transplanted into a child or small adult using a piggyback technique with retention of the recipient vena cava. The left hepatic vein is anastomosed to the Vol. 229 • No. 3 Split Liver Transplantation **317**

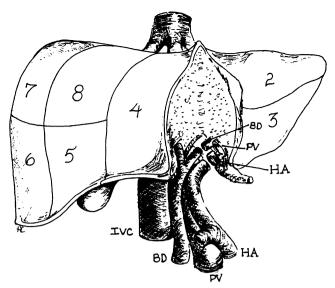


Figure 3. Schematic representation of *in situ* liver splitting. The liver is split between segment 4 and segments 2 and 3 after isolation of the left hepatic artery, left portal vein, and left hepatic vein in the heart-beating cadaver. The left hepatic duct is divided in a sharp fashion before the liver is flushed with University of Wisconsin solution. BD, biliary duct; HA, hepatic artery; IVC, inferior vena cava; PV, portal vein.

suprahepatic vena cava of the patient. However, because of size discrepancy, various venoplasty maneuvers often must be performed to provide a short and patulous anastomosis that is not susceptible to kinking. These techniques have been described by Emond et al.²⁶ Portal vein reconstruction must be individualized to the recipient's anatomy. Often the portal vein of children with biliary atresia is phlebosclerotic and of diminutive diameter. In these cases, a direct end-toend anastomosis is contraindicated, and anastomosis to the confluence of the splenic and superior mesenteric veins is required. In some cases, a vein graft is needed to provide a tension-free anastomosis, but routine use of vein grafts should be proscribed. A review of the techniques of portal vein reconstruction that apply to both LRD and SLT in children has been reported by Saad et al.²⁷ Hepatic artery reconstruction in ex vivo split grafts has varied, depending on whether the common hepatic/celiac trunk is retained with the graft. In this setting, anastomosis is either to the hepatic artery of the recipient or to the aorta with infrarenal iliac conduit. If the left hepatic artery is retained with the left graft, then a microsurgical reconstruction to the proper hepatic artery of the recipient is preferred, as described by Inomoto et al.²⁸ The left graft biliary tract reconstruction is uniformly via a Roux-en-Y left hepaticojejunostomy, with the caveat that in up to 25% of cases there are two or more separate ducts to segments 2 and 3.

Although the *ex vivo* split, as described above, is the most widely used method to transplant two patients with one liver, there are drawbacks to this approach. *Ex vivo* splitting of the liver allograft on the bench is a lengthy procedure and thus results in a long ischemic interval. This takes on more significance if a second recipient operating room is not

available, or if a split graft is transported to another center. Extended cold ischemic times and the required dissection and manipulation of the graft compound the deleterious effects of ischemia alone. Prolonged cold storage has also been associated with increased cytokine release and MHC class II antigen expression, 29,30 leading to an increased inflammatory response on reperfusion. During the separation process into right and left grafts, some allograft rewarming occurs; even if slight, it has been found to be associated with increased susceptibility to hepatic ischemic/ reperfusion injury.31 The collective impact of prolonged ischemia and rewarming during the ex vivo split results in graft injury, which predisposes to a high incidence of poor function unless the organ is placed in a very favorable environment. In the nonurgent patient, unfavorable operative and recipient factors can be minimized, thus decreasing the incidence of poor graft function, as shown by Rela et al.²² Thus, the ex vivo technique may be relegated to the elective case, particularly in adult recipients.

IN SITU TECHNIQUE

A modification of the ex vivo splitting technique is in situ splitting, an extension of the techniques established for LRD procurement that is practiced in the heart-beating cadaver donor. At UCLA, we first attempted in situ SLT in 1992. Our initial experience was not favorable, with only one of four grafts surviving. Causes of failure were primary nonfunction (1), multiple organ system failure (1), and graft torsion (1). However, after establishing an LRD program and accruing an experience of 30 cases, we resumed the in situ split liver program in 1996. In that same year, Rogers et al³² reported an experience with 14 split grafts that resulted in 6-month patient and graft survival rates of 92.8% and 85.7%, respectively. Further, these authors described a lower rate of biliary complications, intraabdominal hemorrhage, and nonfunction of the right graft compared with other series using the ex vivo split techniques (see Table 1).

As with the *ex vivo* technique, only hemodynamically stable cadaveric multiorgan donors are considered for *in situ* splitting. Standard surgical facilities for a multiorgan procurement are used, and no special equipment is needed. Donor hospitals and other procurement teams are notified as soon as possible of the decision to split the liver *in situ*, and the decision to proceed is based on unanimous agreement by the organ teams. The procedure adds 1 to 1.5 hours to a standard multiorgan procedure.

The initial step in the procedure is to obtain control of the supraceliac and infrarenal aorta and inferior mesenteric vein to permit rapid multiorgan cooling in the event of donor instability. If on inspection the vascular anatomy and appearance of the liver are suitable, segments 2 and 3 of the liver are mobilized as in an living donor procurement.³³ The left hepatic artery is mobilized throughout its length. The left portal vein is dissected with ligation of branches to the caudate lobe (segment 1) and to segment 4. Extrahepatic

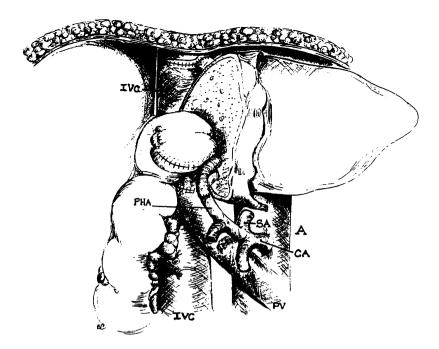


Figure 4. Schematic representation of the implantation of the left lateral segment liver allograft. The patient's vena cava is left intact. The donor left hepatic vein is sutured to the confluence of the recipient middle and left hepatic veins after the right hepatic vein is oversewn. The donor left portal vein is sutured to the recipient portal vein, and the donor left hepatic artery is anastomosed to the recipient common hepatic artery in a microvascular manner without extension grafts. The biliary tract is reconstructed using a Rouxen-Y hepaticojejunostomy. The donor and recipient falciform ligaments are reapproximated to prevent torsion of the liver allograft. A, aorta; CA, celiac axis, IVC, inferior vena cava; PHA, proper hepatic artery; PV, portal vein; SA, splenic artery.

isolation of the left hepatic vein is accomplished with care to ensure that the middle hepatic venous drainage of segments 4, 5, and 8 is not obstructed. Transection of the parenchyma is performed in a line 0.5 to 1 cm to the right of the umbilical fissure, as described for *ex vivo* splitting, and accomplished using electrocautery. The left hilar plate and bile ducts are divided sharply with scissors so as not to devascularize the duct. The middle hepatic vein is retained with the right graft. On completion of the dissection, two liver grafts are procured, each with a preserved vascular pedicle and venous drainage in a bloodless field (Fig. 3).

The procurement proceeds in a standard fashion with perfusion of the abdominal organs with UW solution. After perfusion, the vascular attachments between each graft are divided, leaving the hepatic/celiac arterial trunk, main portal vein, and common bile duct with the right graft. The right graft is prepared on the bench in the standard manner, and the stumps of the left hepatic artery, portal vein, and bile duct are oversewn individually. The left graft usually needs no additional tailoring before implantation.

Concern for the viability of segments 1 and 4 after liver splitting has been voiced by several groups. ^{19,22,31} Opinions regarding the need to resect segments 1 and 4 from the right graft because of devascularization have ranged from always²² to never. ²⁵ It is clear that when dissecting the left hepatic artery, branches to segment 4 are encountered and often ligated. These vessels appear to be more easily identified and preserved during the *in situ* method. Further, because the *in situ* procedure is performed in the heartbeating cadaveric donor, the perfusion of segment 4 can be readily assessed. However, in both *ex vivo* and *in situ* splitting, segment 4 hypoperfusion is a potential pitfall and may require treatment with segmentectomy. If there is any

question about the viability of segment 1, it should be removed at the completion of graft placement.

Implantation of the right graft procured by the *in situ* technique is accomplished identically to a standard orthotopic transplant in which the main hepatic artery, portal vein, and bile ducts are retained by the right graft. The left liver allograft is transplanted in a fashion similar to that used in LRD,³³ including microvascular reconstruction of the hepatic artery (Fig. 4).

SIZE MATCHING IN SPLIT LIVER TRANSPLANTATION

In SLT, graft size must be considered both in terms of fit into the recipient and providing sufficient functional hepatic mass. As has been learned from the RLT experience, donor/ recipient weight ratio is useful as a guide in determining which portion of the liver is suitable for a child. In general, if the ratio exceeds 5 to 10:1, the upper limit of graft volume that can be accommodated by a small child is a segment 2 and 3 graft. Lesser ratios permit the use of a left or right lobe graft.³⁴ From a practical point of view, in most children a left lateral segment is a good size fit. However, in 10% to 20% of cases, the segment 2 and 3 graft is oversized after reperfusion, thus precluding abdominal closure without a prosthesis or with skin alone.³⁵ Despite the guidelines offered by the donor/recipient weight ratio, there is no substitution for an experienced surgeon's visual assessment of the recipient and the graft to be implanted.

Several guidelines^{19,35} have been proposed for the liver size required to sustain hepatic function in a given patient. Volumetric computed tomographic scanning of the lobe of the liver to be transplanted can provide an accurate assessment of the

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Table 2. UCLA PATIENT AND GRAFT SURVIVAL. IN SITU SPLIT

	Number	Percent
Total patient survival	59/65	90.7
Right recipient survival	29/34	85.2
Left recipient survival	30/31	96.7
Total graft survival	58/72	80.5
Right graft survival	31/36	86.0
Left graft survival	27/36	75.0

liver volume. A ratio of graft volume to standard liver volume of >30% is essential for adequate hepatic function.³⁶ Although formulaic calculation of sufficient graft volume may be possible for LRD transplantation, it is impractical when splitting a cadaveric donor, when time and resources may not be available. In this latter setting, a graft with a volume approximately 1% to 1.5% of the body weight of the recipient is large enough to provide excellent hepatic reserve. Segments 2 and 3 of an adult will support a child weighing 6 to 20 kg. For an adult recipient, a left lobe graft from a donor of the same weight will provide approximately 30% to 35% of standard liver volume, which can sustain good liver function. Again, surgical experience is invaluable for making these crucial assessments at the time of liver harvest.

RESULTS OF IN SITU SPLITS

There have been only a few published reports of in situ SLT^{25,32,37} because the procedure has been performed only during the past 3 years. Results from these series have shown improvement over the ex vivo experience, with increased patient and graft survival rates and a lower incidence of technical complications associated with the hepatic artery, biliary anastomosis, and postoperative hemorrhage.²⁵ The patients transplanted with an ex vivo split, as reported by the King's College Group, 22 have been the only series that matched the in situ split results; however, of these 41 patients transplanted with ex vivo splits, all cases were elective except for 4 children and 1 adult (12%) who were classified as emergent. This contrasts with the in situ experience, in which there were substantially more emergent cases. In the UCLA series, 25 38.5% of patients were United Network for Organ Sharing (UNOS) status I (intensive care unit) and 19.2% UNOS status 2 (hospitalized), whereas in the Hamburg series, 32 21.4% were UNOS status 1 and 14.2% UNOS status 2.

An expanded series of in situ split liver grafts performed since July 1, 1996, at UCLA has confirmed these improved results, even in the face of a more urgent group of patients. As of March 1, 1998, we have transplanted 65 patients with a total of 72 in situ split grafts. Of these, 27 (41.5%) were UNOS status 1, 16 (24.6%) UNOS status 2, and 22 (33.8%) elective or UNOS status 3. Patient and graft survival rates are shown in Table 2; patient and graft survival rates for

Table 3. PATIENT SURVIVAL BY UNOS STATUS. UCLA IN SITU SPLIT

Status	Number	Percent
1	23/27	85.2
2	14/18	87.5
3	22/22	100

children are 96.7% and 75%, respectively. Survival stratified to UNOS status is shown in Table 3. Complications are shown in Table 4.

The patient survival rate (90.7%) obtained with in situ splitting is comparable to the best results (90%) reported for ex vivo splitting. However, in the former urgent cases represented 41.5% versus 12% in the latter. Further, the incidence of biliary complications, which seem to be inherent in the ex vivo split technique, occurring in 14.6%²² to 40%,³⁸ is dramatically reduced to <3% with the in situ split operation. Similarly, reoperation as a result of bleeding occurs in up to 20% of patients with ex vivo splitting and in <3% for in situ splits. To date we have encountered no necrosis of segment 4, a frequent complication of ex vivo splitting.

Despite these excellent results, we are disturbed by an 8.3% incidence of primary graft nonfunction, which occurred equally between left and right grafts in six patients. Four of the cases of primary nonfunction occurred early in our experience in patients who received grafts from two donor livers that, in retrospect, were not ideal livers for splitting. Further, half of these occurred in UNOS status 1 patients, whose unfavorable recipient factors affected graft function, as is seen in whole-organ cadaveric grafts.

Although there are advantages to in situ splitting of the liver, as demonstrated above, the technique places an additional burden on the donor hospital and other procurement teams by increasing the operation time by up to 2 hours. If most procurements are regional, a preemptive educational program that presents the benefits of in situ splitting will defuse the objections to the procedure and allow its broader application. This has been realized in our own region, where a proposal has been made to our two organ-procurement agencies to consider all hemodynamically stable multiorgan

Table 4. **COMPLICATIONS OF 72 IN SITU SPLIT TRANSPLANTS**

Complication	Number	Percent	
Hepatic artery thrombosis	2/72	2.8	
Portal vein thrombosis	1/72	1.4	
Biliary leak or stenosis	2/72	2.8	
Reoperation for bleeding	2/72	2.8	
Primary nonfunction*	6/72	8.3	

^{* 50%} UNOS status 1; 4 of 6 grafts harvested from same 2 donors

Table 5. CRITERIA FOR IN SITU SPLIT DONORS

- Hemodynamically stable, heart-beating, cadaveric multiorgan donor
- Age 10–35?
- Minimal to moderate vasopressors (i.e., dopamine < 15 mcg/kg/min)
- Hospitalization <5 days
- Liver function test (excluding prothrombin time) abnormality no greater than 3× normal
- Serum Na < 160 mg/dl

donor candidates between ages 10 and 30 for *in situ* splitting. Full realization of this policy in the greater Los Angeles area should provide an additional 65 grafts per year.

SPLIT LIVER POLICY: IMPACT ON WAITING TIME

A consensus-based policy to split all suitable donor livers would have a substantial impact on the recipient waiting time. In the Paul Brousse experience, 19 the number of transplantable grafts was increased by 28%. Improved use and transplant efficiency has also been reported by the Hamburg group³² and UCLA.²⁵ If these improvements in donor resource use can be extended to the national liver donor pool, the effects would be dramatic. The number of livers suitable for splitting ranges from 15% to 25% of the available donors. In 1996, 4058 livers were transplanted in the United States.⁸ Assuming that 20% were split, an additional 811 grafts would be available for transplantation. Maximal use of this modality would provide enough grafts to supply the entire pediatric waiting list in the United States. This effect on pediatric transplantation has been demonstrated at UCLA. Since implementation of a policy to split every suitable liver, we have decreased the waiting list for children younger than 1 year from 128 days to 24 days: for children older than 1 year, the waiting time has decreased from 192 days to 30 days. Further, use of split livers will benefit the small blood group O recipient, the perennial laggard on the transplant waiting list.

APPLICATION OF SPLIT LIVER TRANSPLANTATION

Based on the data analyzed in this review, we propose that all hemodynamically stable multiorgan donors who fulfill the criteria in Table 5 should be considered as candidates for split liver donation. We believe that the *in situ* technique is superior because it consistently provides two allografts of optimal quality for both adult and pediatric recipients. Further, the grafts obtained with the *in situ* method have proven successful even in urgent patients, and have demonstrated a lower incidence of complications (e.g., biliary and take-back for bleeding). In addition, grafts pro-

cured using the *in situ* technique are likely to be more suitable for sharing among adults because of reduced ischemic injury. However, there are some logistical drawbacks with the *in situ* split, particularly in relation to donor hospital inconvenience and reticence of other organ-procurement teams to acquiesce to the additional time taken for the procedure. In these circumstances, standard organ procurement followed by *ex vivo* splitting should be performed by a team with experience and expertise in major liver resections, RLT, and LRD. Transplantation with two grafts obtained after *ex vivo* splitting will provide excellent results in the elective patient, as previously shown. ^{19,21,22}

Split liver transplantation is now recognized as a practical and meaningful procedure that can truly expand the donor pool. Based on the cumulative experience with this technique, it should now become a routine part of the experienced liver transplant center's armamentarium.

References

- Emond JC, Whitington PF, Thistlethwaite JR, et al. Transplantation of two patients with one liver: analysis of a preliminary experience with split-liver grafting. Ann Surg 1990; 212:14-22.
- Bismuth H, Houssin D. Reduced-size orthotopic liver graft for liver transplantation in children. Surgery 1984; 95:367-370.
- Emond JC, Whitington PF, Thistlethwaite RJ, et al. Reduced-size orthotopic liver transplantation: use in the management of children with chronic liver disease. Transplantation 1989; 10:867–872.
- Broelsch CE, Emond JC, Thistlethwaite RJ. Liver transplantation with reduced-size donor organs. Transplantation 1989; 45:519-523.
- Jurim O, Csete M, Gelabert H, et al. Reduced-size grafts: the solution for hepatic artery thrombosis after pediatric liver transplantation. J Pediatric Surg 1995; 30:853–855.
- Houssin D, Soubrane O, Boillet O, et al. Orthotopic liver transplantation with a reduced-size graft: an ideal compromise in pediatrics. Surgery 1992; 111;532-542.
- Langas AN, Marujo WC, Inagaki M, et al. The results of reduced-size liver transplantation including split livers in patients with end-stage liver disease. Transplantation 1992; 53:387-391.
- United Network for Organ Sharing (http://wwwew3.att.net/UNOS) UNOS Web site 1998.
- Raia S, Nery JR, Mies S. Liver transplantation from live donors. Lancet 1988; 2:497.
- Strong RW, Lynch SV, Ong TN, et al. Successful liver transplantation from a living donor to her son. N Engl J Med 1990; 322:1505-1507.
- Hashikura V, Makuuchi M, Kawasaki S, et al. Successful livingrelated partial liver transplantation to an adult patient. Lancet 1994; 343:1233-1234.
- Kawasaki S, Makuuchi M, Matsunami H, et al. Living-related liver transplantation in adults. Ann Surg 1998; 227:269-274.
- 13. Broelsch CE. Personal communication, 1997.
- Pichlmayr R, Ringe B, Gubernatis G, et al. Transplantation einer spenderbeber auf zwei empfanger (splitting-transplantation): eine neue methode in der weiterentwicklung der lebersegment transplantation. Langenbecks Arch Chir 1988; 373:127-130.
- Bismuth H, Marino M, Castaing D. Emergency orthotopic liver transplantation in two patients using one donor. Br J Surg 1989; 76:722– 724
- Broelsch CE, Emond JC, Whitington PF, et al. Application of reducedsize liver transplants as split grafts, auxiliary orthotopic grafts and living related segmental transplants. Ann Surg 1990; 214:368-377.
- 17. Busuttil RW, Shaked A, Millis M, et al. One thousand liver transplants: the lessons learned. Ann Surg 1994; 219:490-499.

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de Ville de Goyet J. Split liver transplantation in Europe 1988–1993.
 Transplantation 1995; 59:1371–1376.

- 19. Azoulay D, Astarcioglu I, Bismuth H, et al. Split liver transplantation: the Paul Brousse policy. Ann Surg 1996; 224:737–748.
- Otte JB. Is it right to develop living related liver transplantation? Do reduced and split livers not suffice to cover the needs? Transpl Int 1995; 8:69-73.
- Kalayoglu M, D'Alessandro AM, Knechtle JS, et al. Preliminary experience with split liver transplantation. J Am Coll Surg 1996; 182:381–387.
- Rela M, Voregas V, Miniesan P, et al. Split liver transplantation: King's College Hospital experience. Ann Surg 1998; 227:282–288.
- Otte JB, de Ville de Goyet J, Alberti D, et al. The concept and technique of the split liver in clinical transplantation. Surgery 1990; 107:605-612
- Rat P, Paris P, Friedman S, et al. Split liver orthotopic liver transplantation: how to divide the portal pedicle. Surgery 1991; 112: 522-526.
- Goss JA, Yersiz H, Shackleton CR, et al. In situ splitting of the cadaveric liver for transplantation. Transplantation 1997; 64:871–877.
- Emond JC, Heffron TG, Whitington PF, et al. Reconstruction of the hepatic vein in reduced-size hepatic transplantation. Surg Gynecol Obstet 1997; 176:11–17.
- Saad S, Tanaka K, Inomata Y, et al. Portal vein reconstruction in pediatric liver transplantation from living donors. Ann Surg 1998; 227:275-281.
- Inomoto T, Nishizawa F, Sasaki H, et al. Experience with 120 microsurgical reconstructions of hepatic artery in living related liver transplantation. Surgery 1996; 119:20-26.

- Howard TK, Klintmalm GB, Corer JB, et al. The influence of preservation injury or rejection in hepatic transplant recipients. Transplantation 1990; 49:103–107.
- Takada M, Nadeau KC, Shaw GD, et al. The cytokine-adhesion molecule cascade in ischemia/reperfusion injury of the rat kidney: inhibition by a soluble P-selection ligand. J. Clin Invest 1997; 99: 2682–2690.
- Hertl M, Chartraud PB, West DD, et al. The effects of hepatic preservation at 0 degrees C compared to 5 degrees C: influence of antiproteases and periodic flushing. Cryobiology 1994; 31:434–438.
- Rogers X, Malago M, Gawad K, et al. *In situ* splitting of cadaveric livers: the ultimate expansion of the donor pool. Ann Surg 1996; 224:331–341.
- Tanaka K, Uemoto S, Tkunega Y, et al. Surgical techniques and innovations in living related transplantation. Ann Surg 1993; 217:82–87.
- de Ville de Goyet J, Otte JB. Cut-down and split liver transplantation.
 In Busuttil RW, Klintmalm GB, eds. Transplantation of the liver.
 Philadelphia: WB Saunders; 1996:481–496.
- 35. Superina RA, Strasberg SM, Grieg PD, Langer B. Early experience with reduced-size liver transplants. J Pediatr Surg 1990; 25:1157.
- Lo MC, Fan ST, Chan JKF, et al. Minimum graft volume for successful adult to adult living donor liver transplantation for fulminant hepatic failure. Transplantation 1996; 62:696–698.
- Rogers X, Malago M, Habib N, et al. *In situ* splitting of the liver in heart-beating cadaveric organ donor for transplantation in two recipients. Transplantation 1995; 59:1081–1083.
- Langnas AN, Marujo WC, Inagaki M, et al. The results of reduced-size liver transplantation, including split livers in patients with end-stage liver disease. Transplantation 1992; 53:387–391.